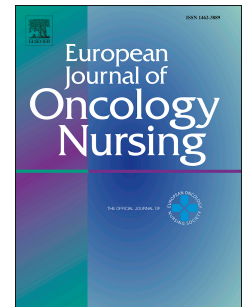


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Emotional Impact and Compassion Fatigue in Oncology Nurses: Results of a Multicenter Study.

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Conflict of interest

No conflict of interest has been declared by the authors.

ABSTRACT

Purpose. To assess the prevalence of Compassion Satisfaction, Compassion Fatigue (Burnout and Secondary Traumatic Stress) and anxiety in oncology nurses and the association with demographics, training, work-related conditions, and psychological factors.

Method. A multicentre, cross-sectional study in 8 selected hospitals in Catalonia (Spain) involving oncology nurses. Primary outcomes were Compassion Satisfaction and Compassion Fatigue (Burnout/Secondary Traumatic Stress), evaluated with the Professional Quality of Life questionnaire v.IV, and anxiety, evaluated with the State-Trait Anxiety Inventory.

Results. Of 297 participants, 18.2% (95% confidence interval [CI]:16.1–20.3) presented low Compassion Satisfaction; 20.2% (95% CI:18.0–22.4), high burnout; and 37.4% (95% CI:34.8–40.0), high Secondary Traumatic Stress. Trait and State Anxiety were high in 5.4% (95% CI:4.2–6.6) and 8.1% (95% CI:6.6–9.6) of participants, respectively. Nurses' desire to leave the unit was associated with high burnout (adjusted odds ratio [ORa] 3.7, 95% CI:1.9–7.5) and Secondary Traumatic Stress (ORa 3.2, 95% CI:1.9–5.3), while the desire to leave the profession was related to high State Anxiety (ORa 12.5, 95% CI:4.6–33.7). Most participants (96.9%) were interested in receiving emotional management training.

Conclusions. Continuous demands on oncology nurses' empathy can lead them to experience compassion fatigue, anxiety and a desire to leave the profession.

The first study carried out with Spanish oncology nurses shows Compassion Fatigue is highly prevalent. This is related to nurses' desire to change units, leave their profession and has negative implications on staff satisfaction and quality of care. This problem justifies institutions support strategies for these professionals.

Keywords. Oncology nurses, Compassion Fatigue, Burnout, Secondary Traumatic Stress, Anxiety, Intention to leave, Nurses' vulnerability.

1 Introduction

Contemporary nursing practice is built around the principle of compassion, defined as the sense of valuing other people and caring about their welfare (Bloom, 2017). Compassion, as the essence of nursing care, improves quality (Straughair, 2012) and response to patients treatment, and affects patients' and professionals' satisfaction with the care experience (Foster et al., 2017; Stamm, 2002). Oncology nurses are the professionals who have most contact with patients and family members when dealing with a cancer diagnosis (Chang et al., 2016), offering emotional support in the face of a potentially poor prognosis and controlling symptoms and side effects. However, nurses may also falsely perceive that they have the means to alleviate their patients' suffering (Duarte and Pinto-Gouveia, 2017a). They face ethical dilemmas related to the obligation to provide treatments they may feel are futile at the end of life, and they are witness to physical pain, suffering, and death (Chang et al., 2016; Austin et al., 2017).

The high emotional demands and negative feelings arising from continued contact with trauma can exceed nurses' self-management capacities, increase their vulnerability, and expose them to pathologies such as depression or anxiety (Sydenham et al., 2017). In this case, health professionals may erect a protective curtain as a coping mechanism against pain, stress and anxiety in the work environment (Gerow et al., 2010), creating an emotional separation between patients and professionals, who adopt an "enduring" behaviour (Morse, 2001) in response to threats. This approach allows nurses to maintain a feeling of control, projecting a façade of strength to "do what must be done", but it also entails emotional suppression and avoidance of empathic commitment.

Joinson (Joinson, 1992) first coined the term Compassion Fatigue (CF) to describe a unique form of burnout. This differentiation of exhaustion related to the care professions, and

especially to nursing, differentiates between the external environment and internal emotional factors, originating from exposure to trauma. Figley (Figley, 2002, Figley, 1995) created a theoretical model based on adaptive or maladaptive responses to stress, establishing four determining factors: capacity to empathize, behaviour toward the victim, difficulty in distancing oneself from work, and satisfaction from caregiving. A prior, non-resolved traumatic experience was also considered a contributing factor. Figley established the association between Secondary Traumatic Stress (STS) and CF, differentiating it from burnout, to describe an array of physiological, psychological, and social symptoms derived from the emotional damage caused by empathic contact with the trauma experienced by others. This type of stress is expressed as a lack of enthusiasm, sadness, irritability, and exhaustion (Figley, 1995), and it is related to anxiety (Lee et al., 2015), physical and psychological disorders, low productivity, absenteeism and the desire to leave the work unit or even the profession (Toh et al., 2012).

More recently, Stamm (Stamm, 2010), based on Figley's conceptual framework, established that professional caregivers' quality of life is determined by the balance between positive and negative emotions. An instrument was developed to measure this concept. The Professional Quality of Life scale (ProQOL) includes three subscales: 1. Compassion Satisfaction (CS), as a positive aspect of care, 2. Burnout and: 3. Secondary Traumatic Stress (STS) as negative aspects of care. According to the author, Compassion Fatigue (CF) is comprised of the latter two subscales. Burnout and STS differ from one another in that the stressors of burnout are related to the organizational work environment and workloads whereas STS is associated with direct exposure to traumatic situations, although their symptomatology is similar and they often appear together (Turgoose and Maddox, 2017; Rossi et al., 2012).

Although all nurses may be vulnerable to emotional stress due to the nature of their work, the intensity of this symptom can differ according to work unit or specialty, and as a function of

personal resilience, patient-related and other environmental factors (Sabo, 2011) . Figure 1 reflects how the ProQOL subscales (Stamm, 2010) bring together these different influential factors described by Sabo. In the same way, the STAI scale differentiates anxiety levels determined by personal traits (Trait Anxiety), from anxiety levels influenced by the environment (State Anxiety). The arrows in Figure 1 show the correspondence between subscales.

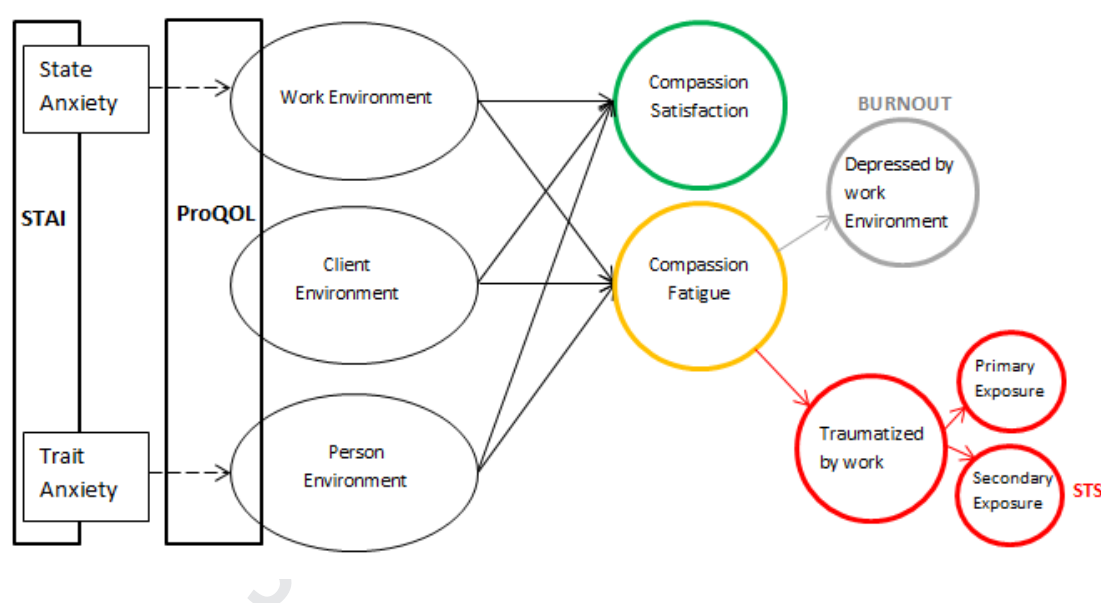


Fig 1. Theoretical path analysis (Stamm, 2010), adapted by authors.

In a systematic review, Beck found that CF was present in 25% of forensic nurses and 78% of palliative care nurses (Beck, 2011). This contrast suggests that oncology and palliative care teams may face specific challenges (Wu et al., 2016) that increase their risk of CF (Mooney et al., 2017a). Between-study heterogeneity in terms of design, methods and instruments means that study results are not always directly comparable, but different reports consistently describe a high prevalence of CF in cancer nurses, regardless of whether they are

working as part of multidisciplinary (O'Mahony et al., 2016) or specialized (Duarte and Pinto-Gouveia, 2017b) teams.

A Spanish study (Sansó et al., 2015), has shown that an average of 41.0% of staff members in palliative care units presented with CS; 12.4% presented with CF; and 15.6% with burnout. By comparison, in geriatric units, the prevalence of CS has been found to be high (63.0%), with STS being moderate (34.4%), and burnout at low levels (4.8%) across professional categories (Campos Méndez, 2015). Although there are no specific prevalence data about CF or its determinants in cancer nurses in Spain, professionals describe coping with the death of patients as a major stress factor (Ko and Kiser-Larson, 2016); they report low self-efficacy and a desire for more training (Todaro-Franceschi, 2013).

Repeated exposure to suffering affects nurses' quality of life and can impact on them for the future (Mooney et al., 2017b), sometimes increasing their desire to leave the profession (Toh et al., 2012). Given the potential for high financial cost, negative impact on the quality of care (Duffield et al., 2014) and problems for the sustainability of health systems (Mealer and Jones, 2013), it is relevant to assess the prevalence, intensity, and determinants of CF in an oncology nursing context. Our specific aims were to assess the prevalence of Compassion Satisfaction, Compassion Fatigue (burnout and Secondary Traumatic Stress), and anxiety in nurses working in oncology units and the association between these outcomes and other variables, including demographics, training, work-related conditions, and psychological factors.

2. Methods

2.1. Design

A cross-sectional, multicentre study, carried out from January to December 2015.

2.2. *Participants and Settings*

The population were nurses working in eight university hospitals in Spain.

Centres were selected by convenience sampling, selecting hospitals with similar characteristics in terms of professional specialisation .

Nurses who met the inclusion criteria were working in the selected oncology units. Nurses who were on leave or in training at the time of study were excluded.

Sample size was determined on the assumption of maximum indeterminacy, with a confidence level of 95% and a precision of $\pm 5\%$. A minimum sample size of 289 was required.

2.3. *Variables and instruments*

Self-report questionnaires were used to evaluate the primary outcomes;

2.3.1 *Professional Quality of Life scale (ProQOL)*

The Spanish version of the ProQOL scale has three independent dimensions and 30 items related to professional quality of life (Stamm, 2010). Positive aspects are reflected in 10 items of the Compassion Satisfaction domain, the CS subscale (Cronbach' $\alpha=0.87$). Negative aspects are evaluated by means of the 10 items of the burnout subscale (Cronbach' $\alpha=0.72$), plus the 10 items of the Secondary Traumatic Stress subscale (Cronbach' $\alpha=0.80$). Together, these latter two subscales measure Compassion Fatigue (Stamm 2010).

For each item, respondents choose between 5-point Likert scale options. Cut-off points are established for every subscale, which determines and classifies each dimension into three risk levels; low, moderate and high (Stamm 2010).

2.3.2 *State-Trait Anxiety Inventory (STAI)*

The STAI scale comprises 20 items for each of two subscales: Trait Anxiety, defined as individual differences that predispose people to anxiety, and State Anxiety, defined as subjective feelings of tension, apprehension, nervousness, and worry at a given time point. For the Spanish version, Cronbach' α is 0.85 and 0.92 for respective subscale (Spielberger et al., 2011)

We categorized scores from both subscales into the three risk levels established by the author, as we did with ProQOL (low, moderate, and high); and we re-expressed the STAI score on a continuous scale from 0 to 100 (Spielberger et al., 2011)

Both ProQOL and the STAI have been validated and widely tested in healthcare contexts (Galiana et al., 2017; Nimmo and Huggard, 2013; Herrero Sanz et al., 2012; Smart et al., 2014).

Other variables, collected through an ad hoc questionnaire, included demographics (age, sex, family burden), training (specialized training, emotion management training), work-related variables (work shift, weekly workload, years of experience, years in current position), and psychological indicators (perceived need for emotional management, desire to change units, feelings of regret/satisfaction regarding chosen profession and the desire to leave the profession).

2.4. Data Collection

During data collection, a pilot study was undertaken with 47 participants to gauge understanding and the time needed for completion; no changes were necessary.

One nurse per centre was assigned and trained as a study coordinator following receipt of Clinical Research Ethics Committees approval. Eligible oncology nurses received information about the study at face-to-face orientation meetings during each shift, delivered by the

principal investigator and the coordinating nurse of each centre. Each participant received a paper copy of the validated questionnaires (ProQOL and STAI) and the ad hoc questionnaire with sociodemographic questions. Each participant submitted an informed consent form together with the self-completed questionnaires voluntarily during a shift. Reminders were sent until a minimum of 80% of oncology nurses had participated. The questionnaires, referenced anonymously, were returned to a closed box and collected by the coordinating nurse.

2.4. Ethical Considerations

The Clinical Research Ethics Committees of all participating centres' approved the study.

A unitary or grouped Clinical Research Ethics Committees approval was obtained for all participating centres, under the references; C.I. 18/2015; 16/2014; Reg. HCB/2015/0494; Ref. HSCSP 15/087; Ref.: 2014626.

Each participant received written and oral information on the study objectives and an invitation to participate on a voluntary and anonymous basis, in compliance with Spanish law 15/1999 of 13th December on data protection, which aims to ensure appropriate confidentiality and data protection.

2.5. Data Analysis

Outcomes are presented as proportions and means (\pm standard deviation [SD]). As frequency measures we used prevalence with 95% confidence intervals (CIs). We assessed the association between variables through binary logistic regression, choosing variables that showed a significant ($p < .05$) crude association in univariate analysis. Associations from multivariate analyses are expressed as adjusted odds ratios (ORa) and 95% CI. All statistical analyses were performed using SPSS v.20 for Windows.

3. Results

3.1. Demographic profile, professional background and training

Of the entire population (N = 366), 297 nurses participated in the study, equivalent to a response of 81.5%. Their characteristics are summarized in table 1. Respondents were primarily women, and half had dependent family members. Nurses working the morning shift were the most frequent responders, and on average they had completed a third of their working life, with over half of their career spent in their current unit. About 60% had never received any emotion management training, although practically all respondents thought there was a need for it. Half reported having considered transferring to another unit, 21.8% had thought about changing profession, and 85.1% said that they would not choose nursing again if they had the choice.

Table 1. Participant Characteristics

Characteristics	N	% (n/N) or mean \pm SD
Age (years)	288	39.8 \pm 11.0
Gender	297	
Women		86.2% (256/297)
Men		13.8% (41/297)
Family dependents	294	
Yes		46.3% (136/294)
No		53.7% (158/294)
Work shift	297	
Morning		27.9% (83/297)
Afternoon		22.3% (66/297)
Night		23.9% (71/297)
Rotating		25.9% (77/297)
Specialized training	296	
Yes		18.2% (54/296)
No		81.8% (242/296)
Professional work experience (years)	295	13.2 \pm 9.8
Experience in current unit (years)	293	8.8 \pm 7.3
Weekly workload (hours)	293	
< 20		7.8% (23/293)

20-40		80.9% (237/293)
> 40		11.3% (33/293)
Prior training in emotion management	294	
Yes		40.8% (120/294)
No		59.2% (174/294)
Perceived need for emotion management training	295	
Yes		96.9% (286/295)
No		3.1% (9/295)
Has considered changing units	288	
Yes		52.1% (150/288)
No		49.7% (138/288)
Has considered changing professions	284	
Yes		21.8% (62/284)
No		78.2% (222/284)
Wouldn't choose the nursing profession again	289	
Yes		85.1% (246/289)
No		14.9% (43/289)

Abbreviations: SD, standard deviation.

3.2. Compassion Satisfaction, Burnout, Secondary Traumatic Stress, and Anxiety

Table 2 presents the prevalence of the main quality of life and anxiety-related indicators.

Overall, about one in five professionals reported a low level of Compassion Satisfaction; one in five, a high level of burnout; and over one in three, a high level of Secondary Traumatic Stress. The mean state anxiety was 9.0 points higher than trait anxiety (36.4 versus 27.4 on a scale of 0 to 100).

Table 2. Prevalence and Severity of Professional Quality of Life

Scale and Subscale	n	Prevalence (%)	95% CI
<i>Professional Quality of Life questionnaire</i>			
Compassion satisfaction			
<i>Low</i>	54	18.2	14.0–23.1
<i>Moderate</i>	141	47.5	41.7–53.3
<i>High</i>	102	34.3	29.0–40.1
Burnout			
<i>Low</i>	51	17.2	13.1–22.0
<i>Moderate</i>	186	62.6	56.9–68.2
<i>High</i>	60	20.2	15.8–22.4
Secondary traumatic stress			
<i>Low</i>	34	11.4	9.7–13.1
<i>Moderate</i>	152	51.2	48.5–53.9
<i>High</i>	111	37.4	34.8–25.2
<i>State-Trait Anxiety Inventory</i>			
Trait anxiety			
<i>Low</i>	158	53.2	47.4–59.0
<i>Moderate</i>	123	41.4	35.8–47.3
<i>High</i>	16	5.4	3.1–8.6
State anxiety			
<i>Low</i>	119	40.2	34.5–46.0
<i>Moderate</i>	153	51.7	45.8–57.5
<i>High</i>	24	8.1	5.3–11.8

Abbreviations: CI, confidence interval.

3.3. Factors Associated with Compassion Satisfaction, Burnout, Secondary Traumatic Stress and Anxiety

Table 3 shows the factors associated with CS, burnout and STS subscales according to multivariable logistic regression. Low CS, high burnout, and high STS were all associated with having considered transferring to another unit. In addition, high STS was associated with not having specialized training.

A high level of trait anxiety was associated with having considered transfer to another unit.

High state anxiety was associated with having considered a change of profession (Table 4).

Table 3. Factors Associated with Professional Quality of Life Impacts**Professional Quality of Life (ProQOL)**

Characteristics	Low Compassion Satisfaction		High Burnout		High STS	
	Prevalence % (n/N)	ORa (95% CI)	Prevalence % (n/N)	ORa (95% CI)	Prevalence % (n/N)	ORa (95% CI)
Specialized training						
No					40.9% (99/242)	2.6 (1.2–5.4)
Yes					20.4% (11/54)	1
Has considered transferring to another unit						
No	8.0% (11/138)	1	10.1% (14/138)	1	23.9% (33/138)	1
Yes	28.0% (42/150)	3.1 (1.4–6.6)	29.3% (44/150)	3.7 (1.9–7.5)	50.0% (75/150)	3.2 (1.9–5.3)
Would choose the nursing profession again						
No	53.5% (23/43)	1				
Yes	10.6% (26/246)	0.1 (0.1–0.3)				

Abbreviations: CI, confidence interval; ORa, adjusted odds ratio; STS, secondary trauma stress.

Statistical significance set at $P < .05$

Table 4. Factors Associated with Anxiety**State-Trait Anxiety Inventory (STAI)**

Characteristics	High Trait Anxiety		High State Anxiety	
	Prevalence % (n/N)	ORa (95% CI)	Prevalence % (n/N)	ORa (95% CI)
Has considered transferring to another unit				
No	2.9% (4/137)	1		
Yes	12% (18/150)	5.3 (1.2–14.7)		
Has considered changing professions				
No			3.6% (8/75)	1
Yes			11.3% (7/62)	12.5 (4.6–33.7)
Would choose the nursing profession again				
No	23.3% (10/43)	1		
Yes	4.9% (12/245)	0.2 (0.1–0.6)		

Abbreviations: CI, confidence interval; ORa, adjusted odds ratio; STS, secondary trauma stress.

Statistical significance set at $P < .05$

4. Discussion

This study aimed to determine the prevalence of Compassion Satisfaction, burnout, Secondary Traumatic Stress and anxiety in oncological nurses. About half the participants presented moderate levels of CS, burnout and STS. The worst scores were shown on the STS subscale, since a considerable proportion of nurses scored high, and only a small proportion were not affected. Compassion satisfaction presence did not mitigate burnout and CF levels, contrary to what previous evidence suggests (Duarte and Pinto-Gouveia, 2017b). These results are comparable to those from a study in the United States, which showed a prevalence of 33% in burnout and 42% for STS in multidisciplinary palliative care team (O'Mahony et al., 2016). Likewise, results from a Portuguese study showed low satisfaction, high burnout, and high STS in a quarter of participating oncology nurses (Duarte and Pinto-Gouveia, 2017b). Somewhat worse are the results from South Africa, where 55% of oncology nurses showed high satisfaction; 61%, moderate burnout; and 75%, moderate STS (Wentzel and Brysiewicz, 2018).

In our study, many nurses scored high in CS but also scored high in CF, especially in the STS subscale. Negative aspects associated with care appear consistently in the literature, with evidence suggesting that the positive presence of CS cannot always compensate the negative aspects, contrary to the conclusions put forward by Giarelli (Giarelli et al., 2016). The heterogeneity in the literature results could be explained by the contextual differences in organizations, cultures or the staff team compositions between different countries.

With regard to state anxiety, cancer nurses mostly scored in the moderate range of intensity. Mean state anxiety was 9% higher than mean trait anxiety, which could be attributed to variables related to the professional work environment since the questionnaires were completed during the shift.

Our participants had a stronger desire to change their unit or leave the profession altogether than the nurses from 10 European countries described in Heinen's study (Heinen et al., 2013), where these

figures were 33% and 9%, respectively. In our study, the desire to change units or professions was consistently associated with low satisfaction and high burnout, STS, and anxiety. With the exception of the relationship between high STS level and specialized training, we did not identify any other variable related to CS, CF, or anxiety, although several recent studies on cancer nurses do describe greater satisfaction in more experienced nurses (Wu et al., 2016) and greater CF with more years in nursing (Hairung et al., 2016a) and in women (Mooney et al., 2017a).

STS is theoretically attributable only to variables such as self-awareness of emotions and experiences, self-care, and the ability to face death (Sansó et al., 2015), while burnout is thought to be related to different environmental factors such as patient mortality rates (Zajac et al., 2017), team cohesion or institutional support (Wu et al., 2016; Hairung et al., 2016b). Other studies attribute burnout to personal factors, mainly socio-demographic and occupational, gender or shift work (De la Fuente-Solana et al., 2017). The simultaneous influence and interactions between both types of factors in the two constructs have yet to be delineated, but these relationships could explain their joint appearance in our sample. Hence, there is still a need to delve into protective or predisposing factors that inform the design of preventive interventions.

Oncology nurses report frustration, difficulty in self-care, inadequate communication processes, and anger (Watts et al., 2010). Moreover, broad consensus exists among this collective around the need for more research; formal support mechanisms; and training to improve coping strategies, (Watts et al., 2010; Cevik and Kav, 2013) communication, symptom management, and decision-making related to ethical dilemmas, which can derive from spiritual and cultural beliefs (Chang et al., 2016). It is noteworthy that almost all of the oncology nurses said they believed emotion management training was necessary. However, even though a large minority of our participants reported having received this training, we did not observe any association between receipt of training and the degree of burnout or STS. This finding suggests that nurses did not receive effective training, and lot more work could be done to improve emotion management interventions (Duarte and Pinto-Gouveia, 2017b).

CF and anxiety seriously damages health systems, affecting professionals, patients, and institutions, and posing challenges for staff retention. The high prevalence of CF among oncology nurses in this multicentre study represents an important starting point for raising awareness of this problem among both professionals and institutions. Strategies to address CF should take into account the specificities of oncology nursing in order to promote high quality and compassionate care and to increase staff retention.

Professionals should receive training that provides them with the personal skills they need to effectively cope with negative factors in their work environment and to manage their emotions (Toh et al., 2012) and pain. Paired with effective leadership and supportive institutional strategies (Straughair, 2012; Gillman et al., 2015) these interventions could potentially improve professionals' well-being and in turn, patients' satisfaction (Zajac et al., 2017). The severity of the problem observed in our sample, together with the unclear relationship between the constructs and variables and the heterogeneous results from international trials lends support to Hill's conclusion (Hill et al., 2016)^(p131): "There is an urgent need to address the lack of intervention development work and high-quality research in this area".

4.1 Strengths and Limitations of Study

Strengths: Both the ProQOL and STAI questionnaires are widely used and have been validated in the Spanish language. We also piloted the questionnaires in the study population to detect and correct any response errors. The study sample exceeded the minimum size required according to the power calculation ($N = 289$), and the total sample ($n = 297$) from 8 hospitals was diverse and representative of nurses in hospitals across Catalonia.

Limitations: Cross-sectional studies do not fulfil the temporal criterion for establishing causation, but permits exploration of which variables are influencing the vulnerability construct. Moreover, we cannot rule out the possible existence of personal, professional, or institutional confounders that were not controlled for in our analyses. There is also a risk of selection bias, as professionals who were more

sensitive to the phenomenon of CF may have been overrepresented in our volunteer sample. Although the high number of participants and centres was representative of hospital staff in our setting, external validity is limited to hospitals with a similar profile and work environment.

5. Conclusions

Although oncology nurses report high levels of satisfaction with their work, there is also a high prevalence of burnout, STS and anxiety. Thus, the positive feelings of compassion satisfaction are not enough to cancel out the negative emotions contributing to compassion fatigue.

Although high burnout, STS and anxiety are directly related to oncology nurses' desire to quit, the absence of any relationship with sociodemographic, educational or work characteristics makes establishing a risk profile elusive. Indeed, our findings suggest that all oncology nurses are at risk for CF. On the other hand, high STS was associated with a lack of specialized training. Moreover, participants' perceived need for emotion management training was almost unanimous, although we did not observe any benefits of this training for nurses' professional quality of life or anxiety.

Taken together, our findings highlight the need for continued research on individual and environmental factors associated with CF that can guide institutions in designing and implementing adequate preventive, training and support policies.

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Conflict of interest

No conflict of interest has been declared by the authors.

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What we know about the topic?

- Compassion is closely linked to the ability of oncology nurses to develop the therapeutic relationship needed to provide high-quality care to patients, but nurses themselves are emotionally vulnerable due to proximity to the patient's trauma.
- Compassion fatigue and anxiety affect patient satisfaction with the care received and nurses' health, with cost implications in health and social care but no previous study in Spain has analysed compassion fatigue in oncology nurses.

What do our results add?

- Compassion fatigue is present and affects nurses working in oncology units, regardless of personal, educational, or professional characteristics, and is directly linked to professionals' desire to leave the work unit and the profession.
- Virtually all nurse respondents perceived a need to be specifically trained in emotional management.
- Undergraduate, postgraduate, and continuing professional education in emotional management is necessary to provide coping tools for nurses throughout their professional career and developing organizational prevention and support policies should be a priority.

DECLARATIONS OF INTERESTS

PFO – Fernandez-Ortega P., has received honorariums as an advisory member from Vifor Pharma in a topic non related to this study

All authors contributed to the study conception and design, data acquisition and interpretation, and the drafting of the manuscript.

All authors have given final approval for this version to be published.